

Indocyanine Green Angiography Findings in Central Serous Chorioretinopathy

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Abstract : *Background and objectives:* To study the abnormalities in the choroidal circulation in cases of central serous chorioretinopathy (CSC) and to compare it with fundus fluorescein angiography. *Setting and Design:* Prospective, interventional and non comparative case series in a tertiary eye care institute. *Material and Methods:* 40 consecutive cases of CSC were included in the study. A complete clinical ophthalmological examination was performed. Simultaneous fluorescein angiography (FA) and indocyanine green angiography (ICGA) were done using confocal scanning laser ophthalmoscope and the digital images were analyzed. *Results:* FA showed leakage at the level of retinal pigment epithelium in all the cases ($n=40$, 100%) of CSC. Surrounding these leakage points, ICGA demonstrated choroidal filling delay ($n=31$, 77.5%), abnormal choroidal hyperfluorescence ($n=34$, 85%), venous dilatation ($n=24$, 60%) and persistent small localized hypofluorescence ($n=28$, 70%). *Conclusion:* Abnormality of the choroidal circulation in the form of regional vascular hyperpermeability was observed in CSC, which might be attributed to the disease pathogenesis.

Keywords: abnormal choroidal circulation, central serous chorioretinopathy, fluorescein angiography, indocyanine green angiography.

I. Introduction

Central serous chorioretinopathy (CSC) is an idiopathic disease, commonly affecting young male adults, characterized by circumscribed serous sensory retinal detachment mostly confined to the macula. CSC can present as classic acute chorioretinopathy, chronic diffuse retinal pigment epitheliopathy and bullous retinal detachment.[1] A working hypothesis has been postulated stating impaired choroidal circulation, consequent dysfunction of adjoining retinal pigment epithelium (RPE) and accumulation of fluid under the sensory retina altogether causing clinical CSC.[2] The present investigation was undertaken to study the indocyanine green angiography (ICGA) findings of the choroid in CSC and to correlate it with simultaneous fluorescein angiography (FA) findings.

II. Material And Methods

The study was a prospective, interventional case series done at a tertiary eye care centre in North East India. It was approved by the Institutional Ethics Committee and adhered to the Declaration of Helsinki. Written consent was obtained from all the participants. There was no conflict of interest.

Newly diagnosed 40 consecutive cases of acute CSC with clear media were included in the study from May 2011 to April 2013. Patients with history of more than 2 weeks of visual symptoms or any retinal or choroidal pathology other than CSC were excluded from the study. A complete clinical ophthalmological examination was done in all the cases. Diagnosis was done on the basis of clinical findings and simultaneous fundus fluorescein and indocyanine green angiography.

Simultaneous FA and ICGA were performed in all the cases at presentation, with the help of a confocal scanning laser ophthalmoscope (Heidelberg Retinal Angiograph-II, Heidelberg Engineering, Dussenheim, Germany). 25mg of ICG (Aurogreen®, Aurolab) was dissolved in 5ml of 20% fluorescein solution (Vimal Formulation Pvt. Ltd.). The mixed drug was then injected into the cubital vein. Argon laser emitting at 486nm for excitation and filters blocking transmission of wavelengths below 510nm were used for FA. For ICGA a diode laser emitting at 795nm and blocking filters for wavelength below 835nm were used. Digital images were recorded for a minimum period of 15 minutes post injection. The images were analyzed and Heidelberg imaging software (in-built) was used to identify the same region for comparative analysis of FA and ICGA images. In FA, the type, number and location of leaks was investigated; whereas in ICGA, filling delay of the choroidal arteries and capillaries, choroidal venous dilatation, choroidal vascular hyperpermeability (hyperfluorescence) and punctate choroidal hypofluorescence in the areas around the leakages was analyzed.

III. Results

The study group comprised of 40 cases (40 eyes) of acute classic CSC, diagnosed on the basis of clinical presentation, ocular findings, simultaneous FA and ICGA. All the cases were male with duration of symptoms less than two weeks. The mean age was 35.9 ± 3.77 years. FA demonstrated ink blot leak in 34 eyes

(85%) and smoke stack leak in 6 eyes (15%). 37 eyes (92.5%) had single leak and 3 eyes (7.5%) had multiple leaks in FA. 8 eyes (20%) also had retinal pigment epithelial detachment (PED).

Early phase ICGA demonstrated focal areas of filling delays of the choroidal arteries and the choriocapillaris in all the 40 eyes (100%). The affected areas had geographical appearances and were of variable sizes (≥ 1 disc diameter). The filling delays were found persistent till the dye had filled the retinal veins (Figures 1 and 2).

In ICGA focal choroidal hyperfluorescence surrounding the FA leakage points at RPE was observed in 34 eyes (85%). Choroidal hyperfluorescence was most prominently observed in the mid phase and persisted in the late phase with reduced intensity (Figures 3 - 6). Small localized hypofluorescent areas surrounding FA leakage points were also seen in 28 eyes (70%) which remained persistent (from early to late phase) throughout the passage of the dye (Figures 3 and 6). Choroidal venous dilatation was observed in 24 eyes (60%) (Figure 7).

IV. Discussion

ICGA was investigated in CSC by various researchers in active, remission and recurrent stage of the disease.[3-18] ICGA commonly demonstrated impaired choroidal circulation. Previously reported findings during ICGA were filling delay in the choroidal arteries and choriocapillaris[3-8] and choroidal hyperfluorescence.[3-18] Other less commonly reported findings in ICGA were choroidal venous dilatation,[4-6] localized small hypofluorescent areas around the site of focal fluorescein leakage,[3-6] reduction of choroidal blood flow by 45% and decreased foveal choroidal blood flow,[3-18] punctate choroidal hyperfluorescent spots,[12] irregular patchy dye filling of subfoveal choroidal capillaries along with significant time delay and loss of the normal central centrifugal expansion pattern of dye filling.[18] Choroidal hyperfluorescence was considered as a hallmark of the disease occurrence as it remained persistent even after the clinical remission of the disease.[5] Similar hyperfluorescence was observed in the unaffected opposite eye also.[5] The reported incidences of different findings were variable amongst the investigators (TABLE 1). It appeared that the difference in incidences among the studies were dependent on the dose of the ICG dye, angiography method (simultaneous FA & ICGA or at interval), type of the angiography equipment used, method of photographic documentation and stage of the disease.[3,4,6,8,10,11,18] Simultaneous FA and ICGA demonstrated that the areas of choroidal circulatory abnormalities were mostly located under the fluorescein leakage at the RPE.[3]

Pathophysiology of CSC was speculative and controversial. FA demonstrated flow of fluorescein dye from the choroidal circulation to the subretinal space across the RPE through single or multiple leakage points. Animated video of the extracted image also showed abnormal ICG dye filling and propagation of the dye in the choroid in CSC as compared to healthy volunteers.[19] Studies using ICGA also demonstrated various abnormalities in the choroidal circulation. RPE abnormality was unlikely to be the primary pathology as artificially induced isolated single or multiple defects in the RPE could not cause accumulation of subretinal fluid.[20] These facts raised a theoretical debate regarding the primary site of pathology and the role of impaired choroidal circulation in CSC.

In the present study we found filling delay of the choroidal arteries and choriocapillaris in all the cases (100%). In the literature, reported incidence of these findings varied from 63% to 100% (TABLE 1). In our study choroidal hyperfluorescence was found in 34 eyes (85%). The reported incidence of choroidal hyperfluorescence varied from 37% to 100% (TABLE 1). Some authors documented choroidal venous dilatation but its definition was unclear. We had also observed choroidal venous dilatation in 24 eyes (60%). All the patients demonstrated simultaneous fluorescein leak at RPE overlying the area of choroidal hyperfluorescence. Kitaya et al [3] reported hypofluorescent points around the leakage in 27 eyes (75%). In our study, we observed similar findings in 28 eyes (70%).

Precise reason of delay in the filling of choroidal arteries and choriocapillaris was unclear. Kitaya et al[3] and Prunte et al[6] correlated it with raised pressure in the choriocapillaris secondary to venous congestion. In our study, all the cases of choroidal filling delay in ICGA demonstrated fluorescein leakage from the RPE of the adjoining area. Local choroidal congestion, dysfunction of the overlying RPE and subsequent flow of fluid in the subretinal space were accounted for sensory retinal separation and CSC.[3,6] The findings of the present investigation were in agreement with this theory.

Focal choroidal hyperfluorescence was interpreted as regional vascular hyperpermeability.[3,5-11] We also believe the same concept as in our study, focal patchy areas of choroidal hyperfluorescence was observed in 85% cases and in all cases the affected areas were located around the leakage point in FA. These hyperfluorescent patches were best observed in the mid phase of ICGA. These patches enlarged along with time and remained persistent with less prominent hyperfluorescence in the late phase of ICGA. Similar findings were also observed by other investigators.[3,5]

Small localized hypofluorescent areas around the fluorescein leakage were also observed by different workers. The reported frequency of these findings were variable because previously detailed evaluation of small choroidal structures were not possible due to poor resolution of angiography.[3,4,6] Simultaneous angiography

using confocal laser ophthalmoscope has enabled visualization of same regions of the choroid and the retina. We observed localized hypofluorescent areas around the fluorescein leakage points. Kitaya et al[3] reported similar findings. Guyer et al[8] also reported similar findings and described it as ‘occult’ presumed RPE detachment in CSC. Kitaya et al[3] and Prunte et al[6] hypothesized that the hypofluorescent areas were due to occlusion and resultant non perfusion of the choriocapillaris. In our study, the punctate hypofluorescent areas were detected continuously from early to late phase of the ICGA and in agreement with the findings of the previous investigators.[3-6]

V. Conclusion

In conclusion, the present study documented choroidal circulatory disturbance in CSC and it revalidated the previous findings reported by various workers. Further study by depth enhancing and Doppler OCT flowmetry will throw new light on the cause and effect relationship of the above findings.

VI. Figures and Tables

Table 1: ICGA Data in Classic CSC

ICGA Data in Classic CSC							
Sl. No.	Authors	Total No. of eyes (n)	Filling delay in the Choroidal Arteries and Choriocapillaris at the FA leakage point (%)	Focal Choroidal hyperfluorescence (Regional Vascular Hyperpermeability) %		Choroidal Venous Dilatation	
				Surrounding FA leakage point	Away from FA leakage point (%)	Localized around FA leakage point (%)	Entire Posterior Pole (%)
1	Scheider et al ¹¹ (1993)	19	63%	37%	-	-	-
2	Guyer et al ⁸ (1994)	29	Nil	100%	-	-	-
3	Piccolino et al ¹⁰ (1994)	33	Nil	94%	-	-	-
4	Prunte and Flammer ⁶ (1996)	32	100%	59%	-	-	-
5	Iida et al ² (1999)	105	71%	96%	55%	51.5%	9.5%
6	Kitaya et al ³ (2003)	36	100%	83%	47%	Observed but not correlated	-
7	Inoue et al ¹⁶ (2010)	38		100% (Intense - 72% Intermediate - 19% Low - 9%)	-	-	-
8	Jirarattanasopa et al ¹⁷ (2012)	27	72%	100%	-	-	-
9	Present study (2014)	40	100%	85%	-	60%	-
	Other findings:-		i) Iida et al ² - Focal choroidal hyperfluorescence around dilated veins (100%). ii) Kitaya N et al ³ - localized hypofluorescent areas around FA leakage point (75%). iii) Jirarattanasopa et al ¹⁷ - Punctate hyperfluorescent spots (93%). iv) Present study - Localized hypofluorescent areas around FA leakage point (70%)				
	Angiography method and device used:-		<ul style="list-style-type: none"> • Iida T et al² - ICGA done 5 minutes after FA. Dose of ICG dye - 40mg. Roden Stock Scanning Laser Ophthalmoscope. • Kitaya N et al³ - Simultaneous FA and ICGA. Dose of ICG dye - 25mg. Heidelberg Retinal Angiogram. • Jirarattanasopa et al¹⁷ - Simultaneous FA and ICGA. Heidelberg Retinal Angiogram. • Others used digital camera. • Present study - Simultaneous FA & ICGA. Dose of ICG dye - 25mg. Heidelberg Retinal Angiogram - II. 				

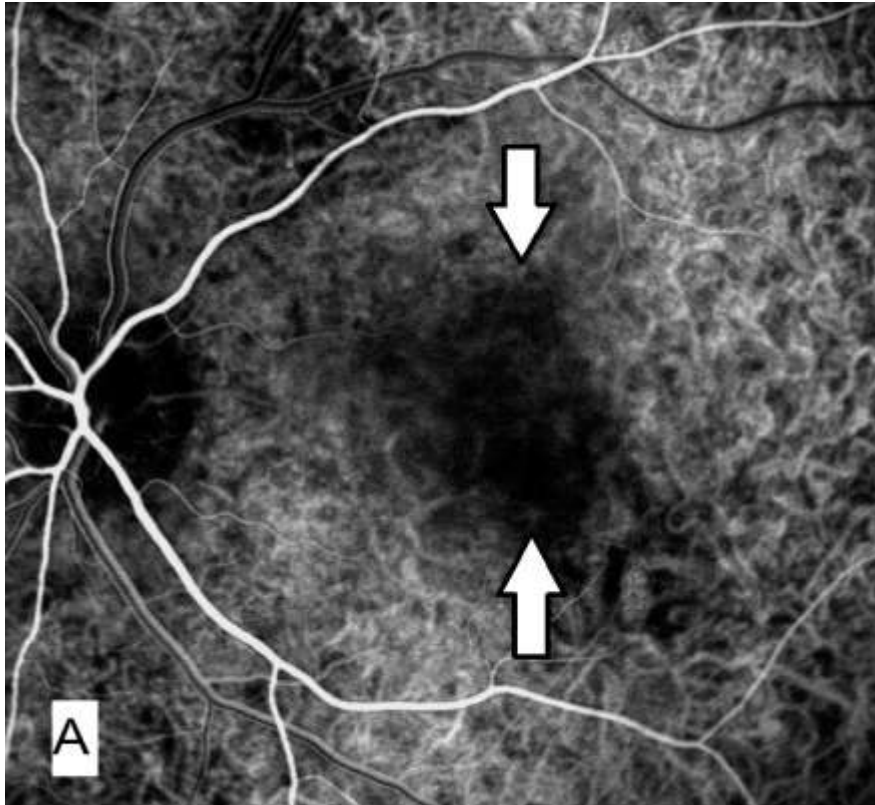


Figure 1 (A) – The left eye of a 30 years old male suffering from CSC with ICGA showing delayed filling of the choriocapillaris (arrows)

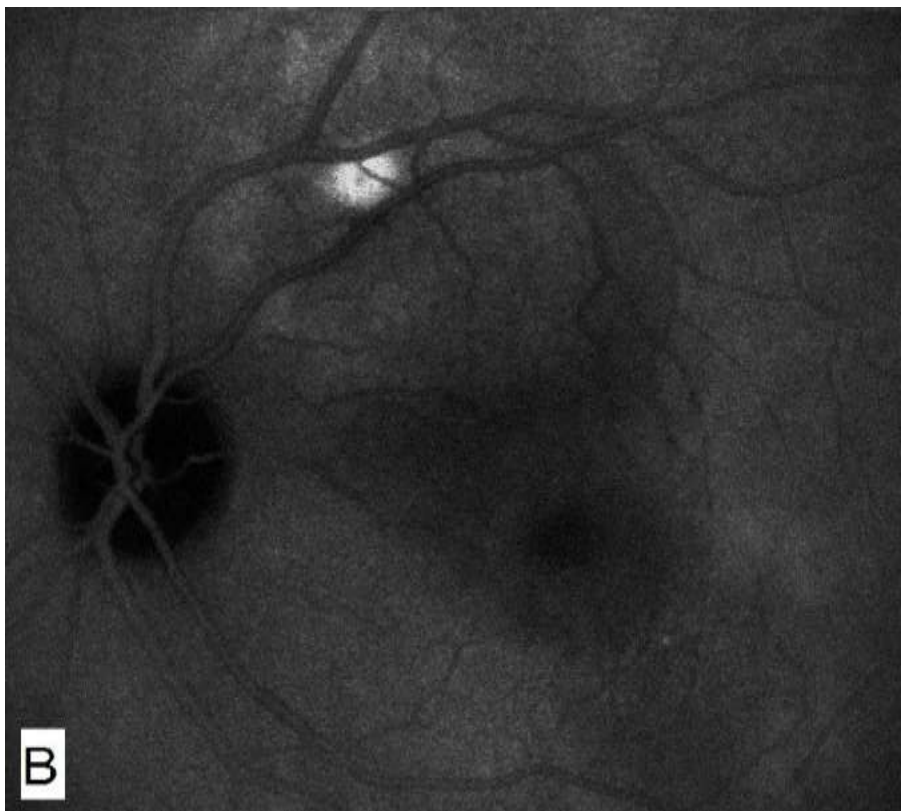


Figure 1 (B)– The left eye of a 30 years old male suffering from CSC with ICGA showing subsequent hyperfluorescence of the same area persistent in the late phase

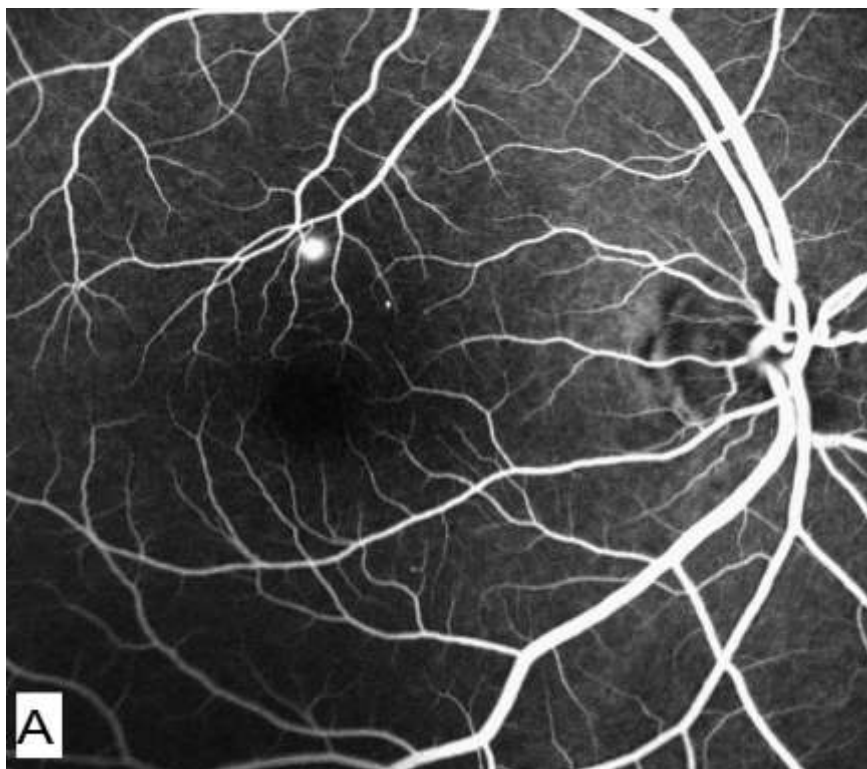


Figure 2 (A) – FA of the the right eye of a 39 years old man suffering from CSC showing leak at RPE level in the overlying area

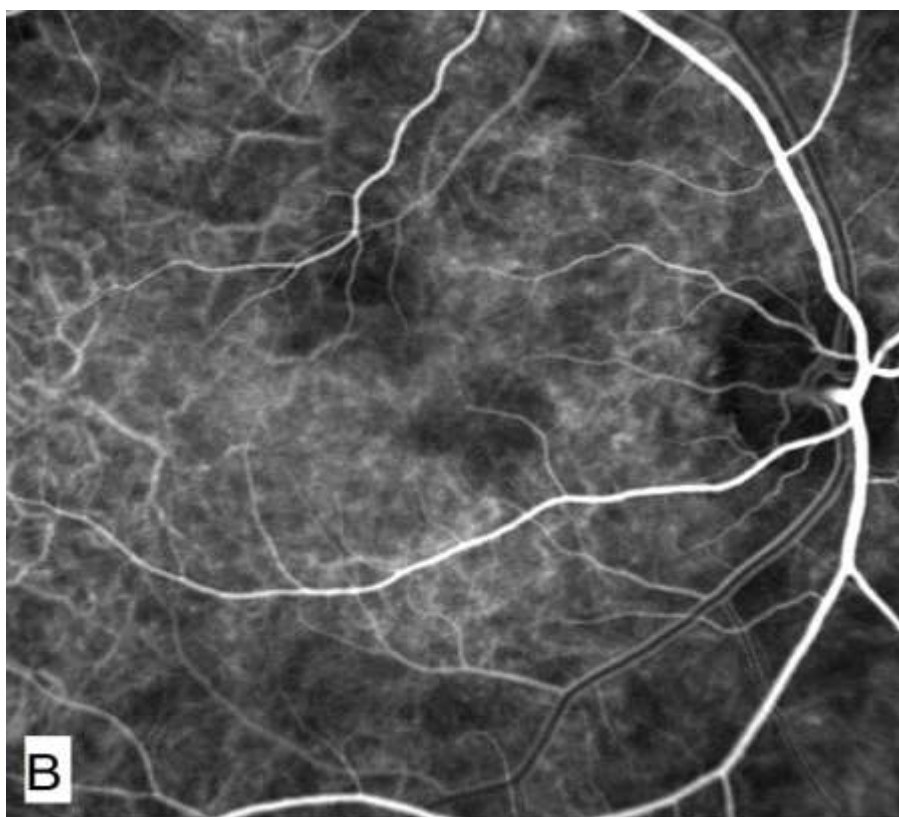


Figure 2 (B) – ICGA of the right eye of a 39 years old man suffering from CSC showing filling delay of the choriocapillaris

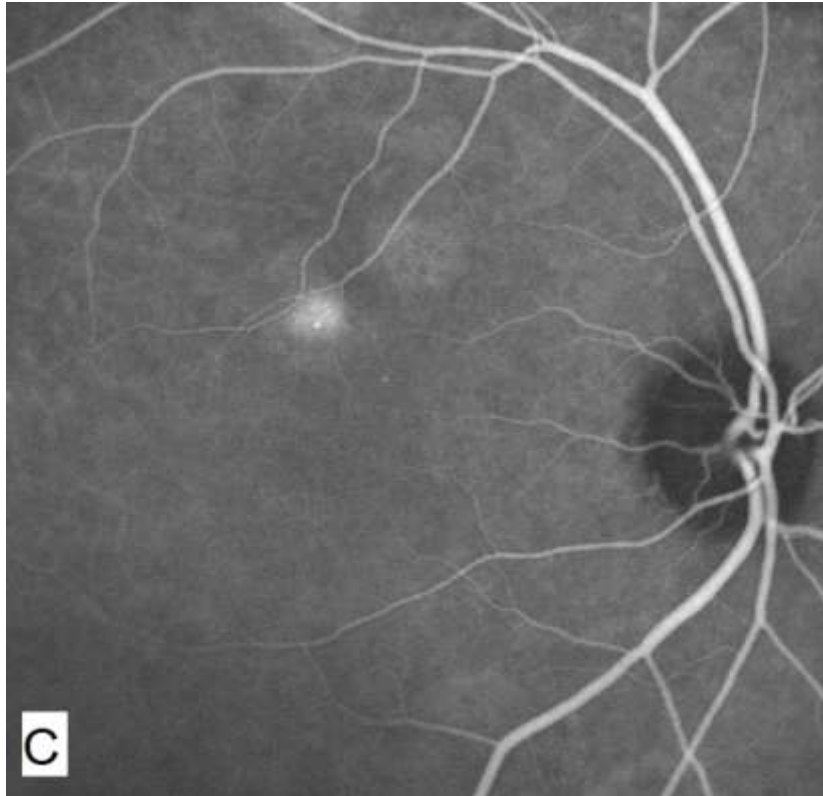


Figure 2 (C) - ICGA of the right eye of a 39 years old man suffering from CSC showing persistent patchy areas of hyperfluorescence in the late phase of ICGA

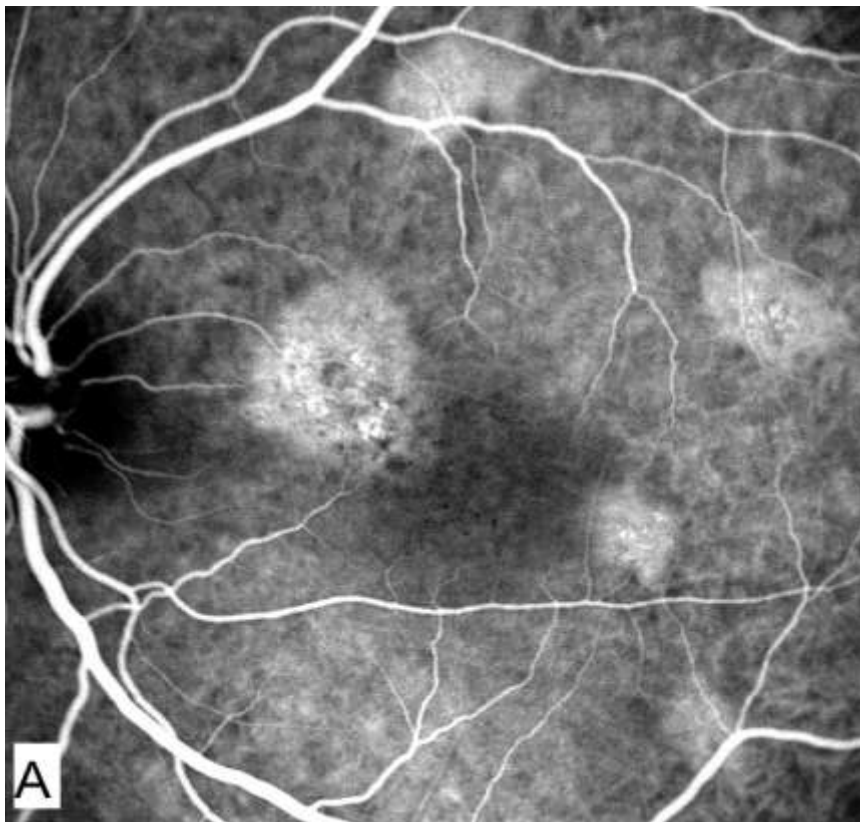


Figure 3 (A)– ICGA findings in a case of 38 years old male suffering from CSC in the left eye with mid phase showing multiple focal patchy areas of hyperfluorescence

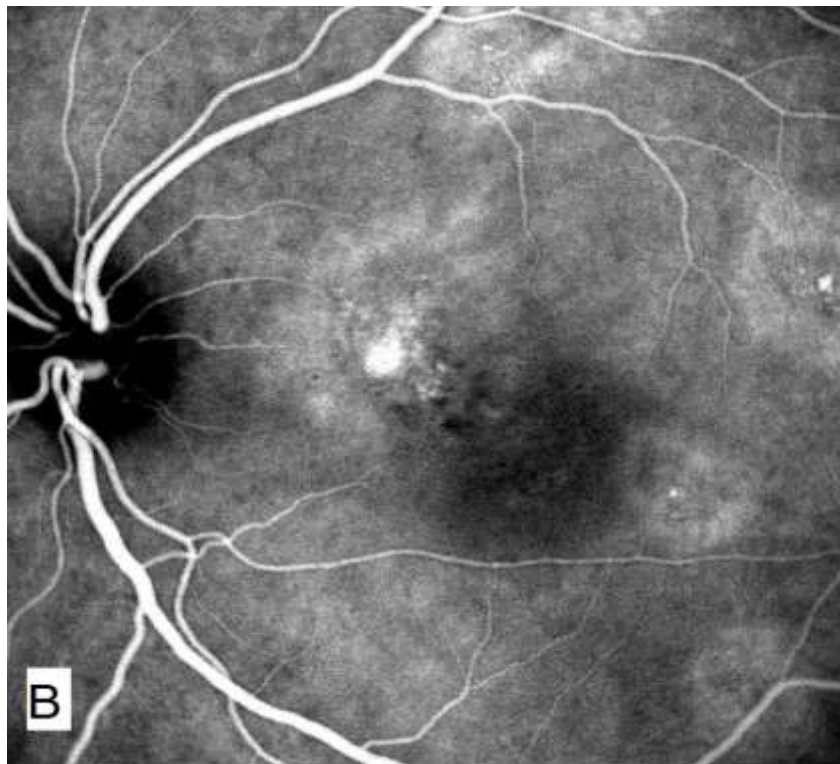


Figure 3 (B) - ICGA findings in a case of 38 years old male suffering from CSC in the left eye showing patchy hyperfluorescent areas increased in size in the late phase but with reduced intensity. However, focal hypofluorescent areas remained persistent.

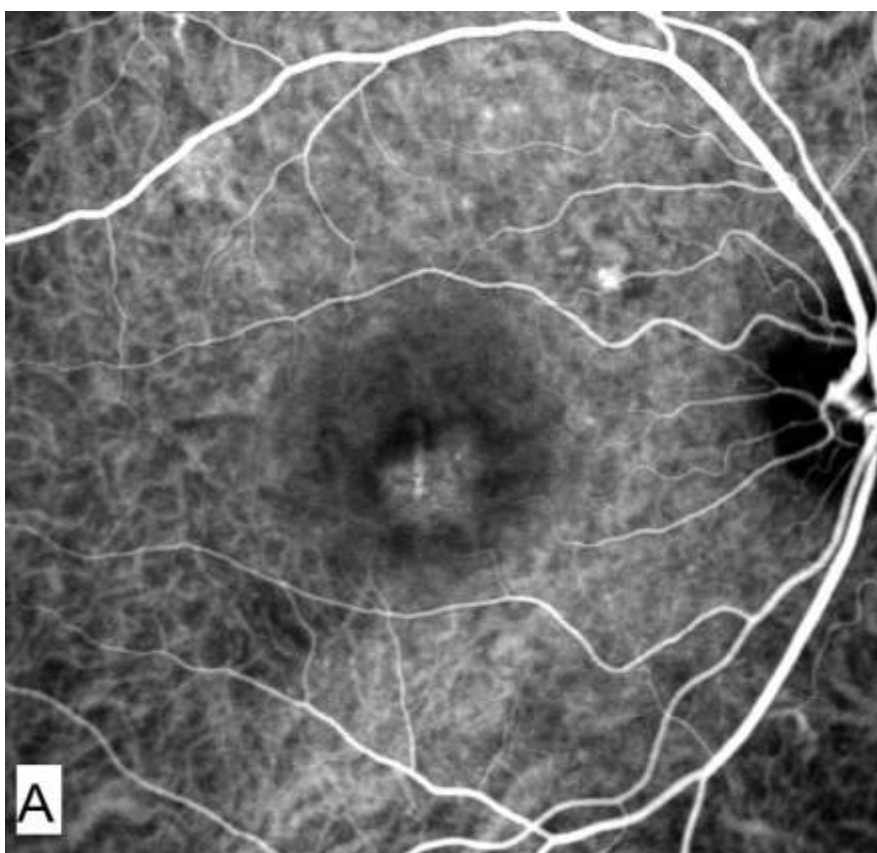


Figure 4 (A) – A 38 years old male suffering from CSC in the right eye with ICGA showing abnormal choroidal hyperfluorescence in early phase

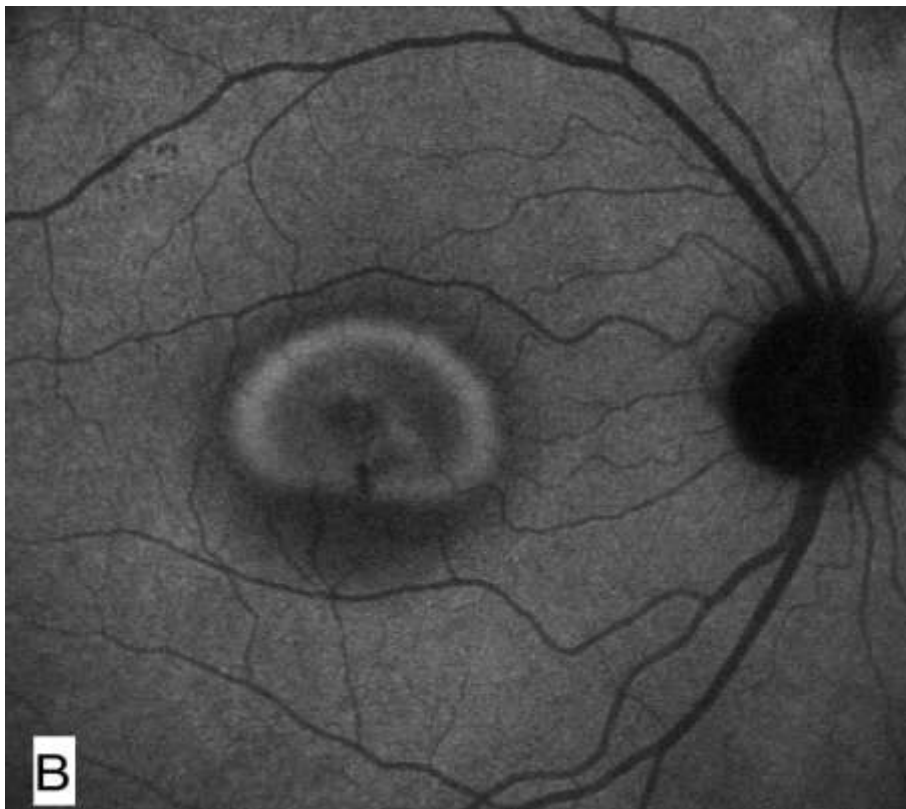


Figure 4 (B) - A 38 years old male suffering from CSC in the right eye with ICGA showing abnormal choroidal hyperfluorescence in late phase.

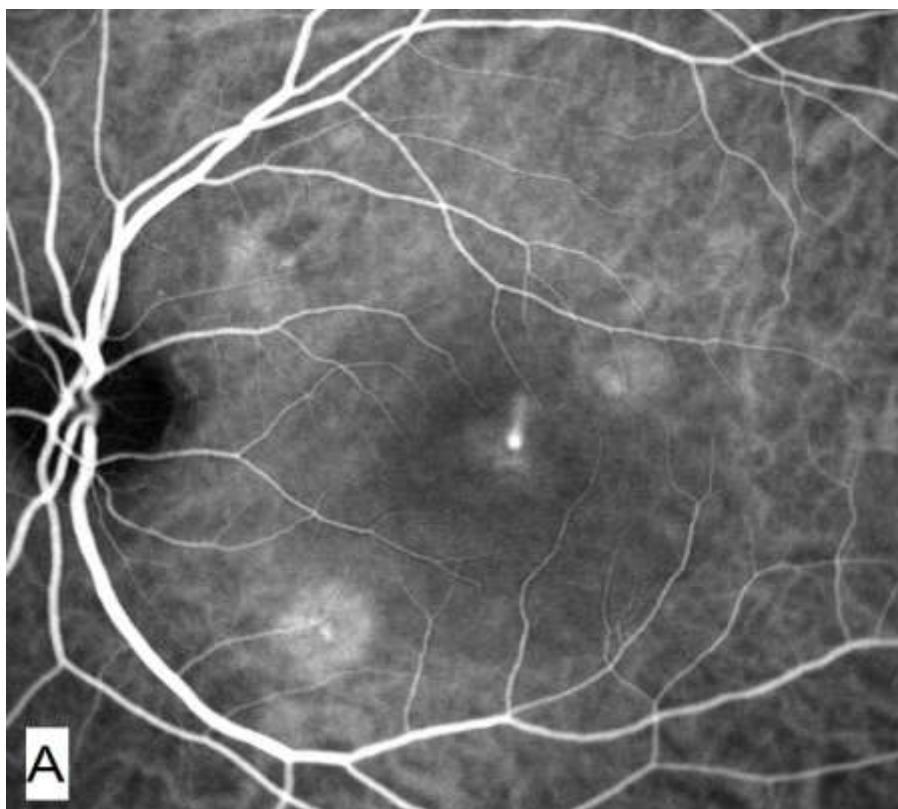


Figure 5 (A) – ICGA of a 38 years old male suffering from CSC in the left eye with mid phase showing abnormal choroidal hyperfluorescence with sensory retinal separation and a smoke stack leak

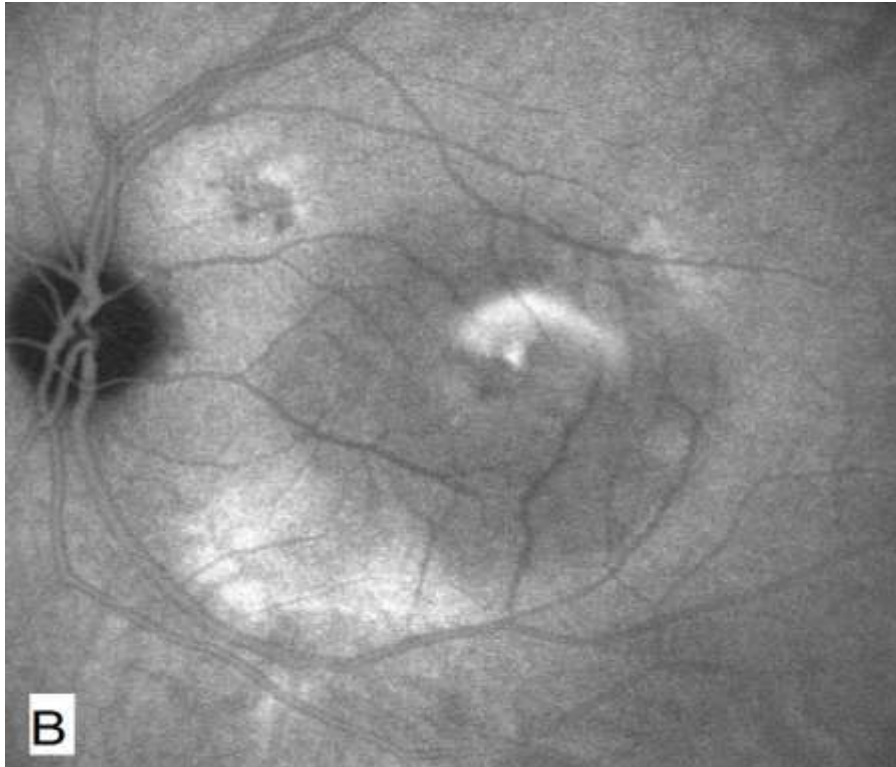


Figure 5 (B) - ICGA of a 38 years old male suffering from CSC in the left eye with late phase showing persistent hyperfluorescence.

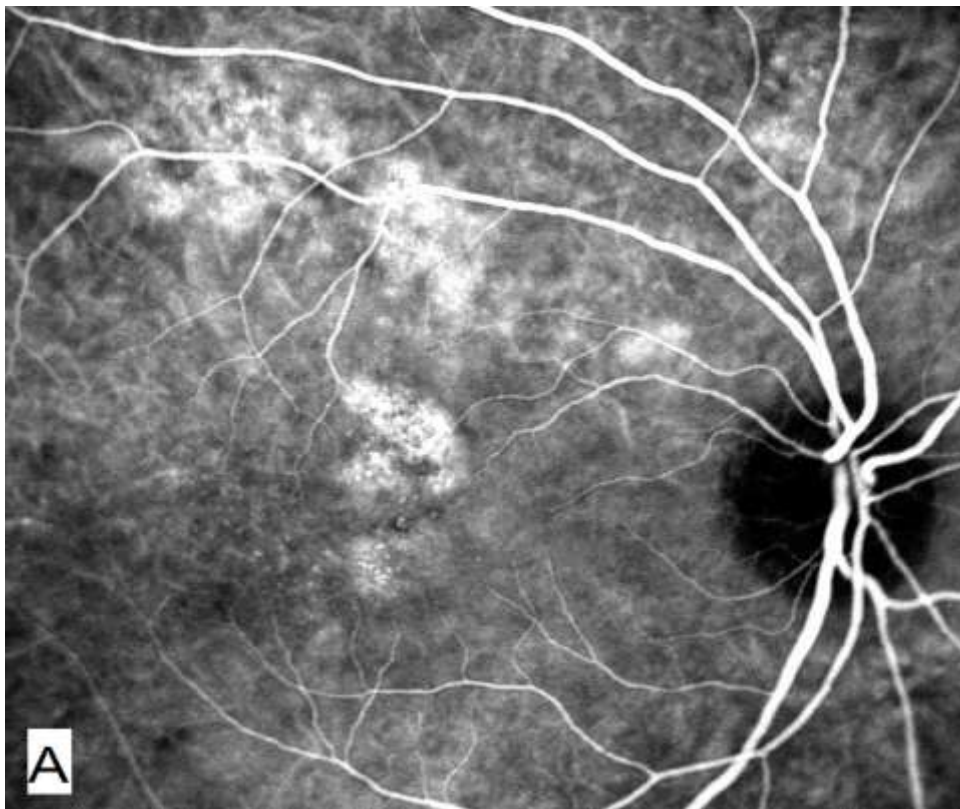


Figure 6 (A) – CSC in the right eye of a 31 years old male with ICGA in the mid phase showing multiple focal patchy areas of choroidal hyperfluorescence and punctate hypofluorescence

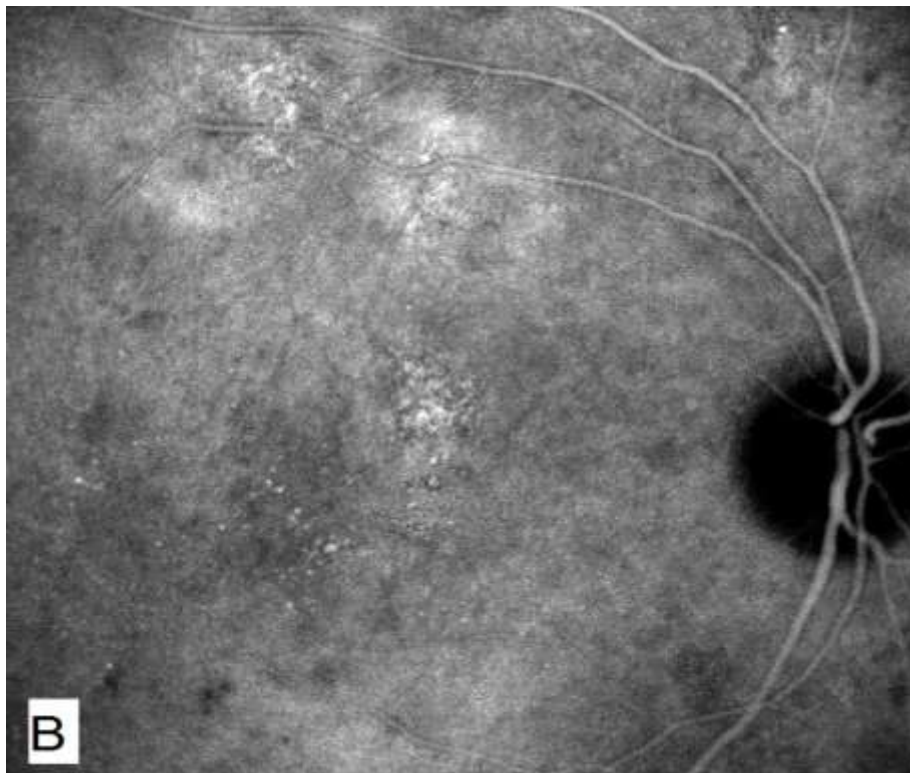


Figure 6 (B) - CSC in the right eye of a 31 years old male with late phase of ICGA showing persistent hyperfluorescent areas with increased size and reduced intensity in the late phase. The punctate hypofluorescent areas were also persistent.

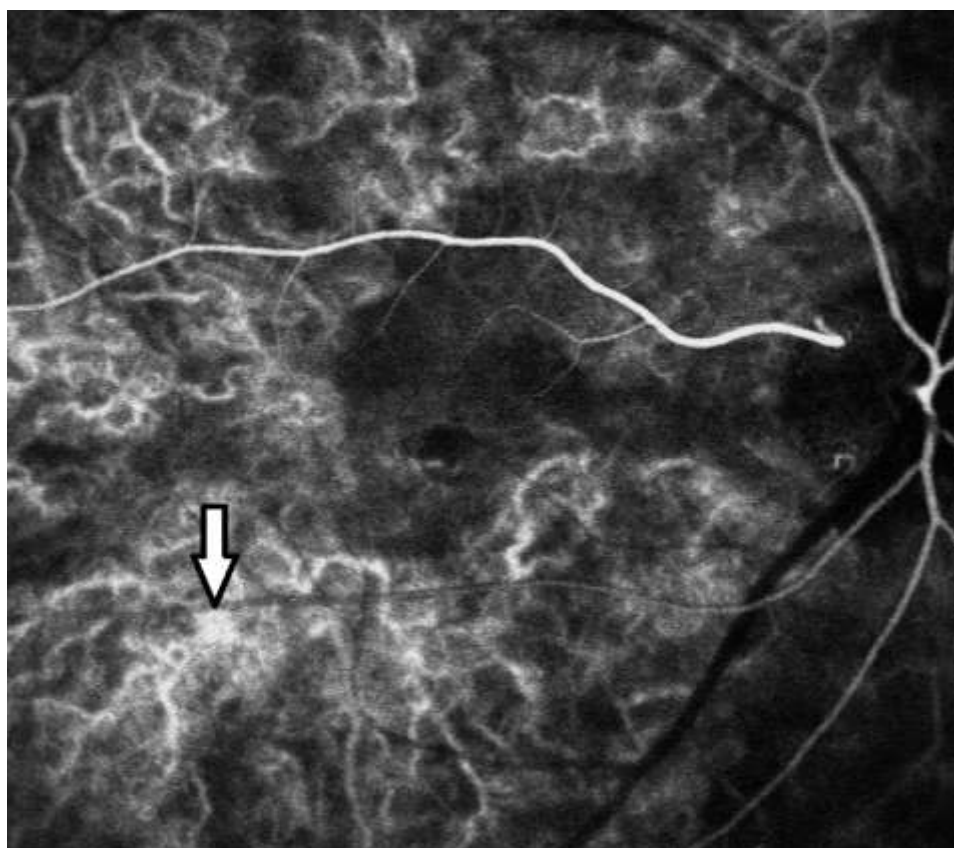


Figure 7 – ICGA in the right eye of a case of CSC (35 years old male) showing venous dilatation (arrow).

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